



Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: guidelines for the evaluation of food allergies.

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: guidelines for the evaluation of food allergies. Gastroenterology 2001 Mar; 120(4):1023-5.

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Food allergy, including immediate (immunoglobulin E-mediated) gastrointestinal reactions to food protein; oral allergy syndrome; dietary protein-induced proctitis/proctocolitis of infancy; dietary protein-induced enteropathy; dietary protein-induced enterocolitis syndrome; gastroesophageal reflux associated with cow's milk allergy in infants; eosinophilic gastroenteritis; eosinophilic esophagitis; enteropathy/malabsorption

GUIDELINE CATEGORY

Diagnosis

Management

Risk Assessment

Treatment

CLINICAL SPECIALTY

Allergy and Immunology

Family Practice

Gastroenterology
Internal Medicine
Pediatrics

INTENDED USERS

Dietitians
Physicians

GUIDELINE OBJECTIVE(S)

To provide a rational basis for the evaluation of food allergy in gastrointestinal disorders

TARGET POPULATION

Individuals with characteristic signs and symptoms of food allergies, including suggestive immunologic responses to proteins in food or biopsy findings, in whom other causes are unidentified (or who fail therapy)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnostic assessment

1. Patient selection for evaluation for food allergy based on epidemiologic factors
2. Immunoglobulin E skin prick or puncture test
3. Immunoglobulin E radioallergosorbent test (RAST)
4. Oral challenge
5. Adjunctive tests, such as endoscopy/biopsy, absorption studies, stool analysis, pH probe

Treatment

1. Elimination diets, including eliminating one or several foods suspected of provoking symptoms; eliminating all foods except a defined group of "allowed" foods (oligoantigenic diet); use of amino acid-based formula (elemental diet)

MAJOR OUTCOMES CONSIDERED

- Predictive value, specificity, and false-positive rate of skin tests and other diagnostic tests
- Symptoms of food allergy
- Diagnostic findings in food allergy
- Incidence of food-allergic reaction, including immunoglobulin-E-mediated and non-immunoglobulin-E mediated reactions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE searches were conducted for peer-reviewed clinical studies of particular disorders using MeSH (National Library of Medicine Medical Subject Headings) terms for the disorder plus the term "food hypersensitivity". In addition, more general searches were conducted for food hypersensitivity disorders.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This document was approved by the Clinical Practice and Practice Economics Committee on September 23, 2000, and by the American Gastroenterological Association Governing Board on November 12, 2000.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

A recent consensus workshop (Workshop on the Classification of Gastrointestinal Diseases of Infants and Children, November 1998, Washington, D.C.) concluded that the diagnosis of food allergy is made on the basis of one or more of the following elements:

- History of an allergic, or allergic-like, reaction to a food ingestion
- Exclusion of anatomic, functional, metabolic, or infectious causes
- Pathologic findings consistent with an allergic cause (usually eosinophilia)
- Confirmation of a relationship between ingestion of the specific dietary protein and symptoms by clinical challenges or repeated, inadvertent, exposures
- Evidence of the food-specific immunoglobulin E antibody in settings of immunoglobulin E-mediated disease
- Failure to respond to conventional therapies aimed at anatomic, functional, metabolic, or infectious causes
- Improvement in symptoms with elimination of the causal dietary protein(s)
- Clinical response to treatments of allergic inflammation (i.e., corticosteroids)
- Similarities to clinical syndromes either proven or presumed to be caused by immunologic mechanisms
- Lack of other explanations for the clinical allergic-like reaction

The selection of patients who may benefit from an evaluation for food allergy also should take into consideration a number of epidemiologic factors that suggest an increased probability of underlying food allergy. Epidemiologic factors that may be helpful in assigning a priori risk for food allergy include:

- Young age of patient (<3 years)
- History of acute reaction proximate to ingestion of a particular food
- Associated atopic diseases, such as atopic dermatitis (eczema), acute food allergic reactions, asthma, and family history of atopic diseases

Of primary importance is the fact that food allergy is rarely confirmed in adults.

In addition to considering the above elements, food allergy should be considered as a potential immunopathophysiologic mechanism in a number of defined gastrointestinal disorders that have clearly been linked with food allergy, at least in a subset of patients. These particular disorders and symptom complexes are:

Clear relationship, high risk

- Acute, severe (sometime multisystem) gastrointestinal reaction immediately after ingestion ("gastrointestinal anaphylaxis")¹
- Oral allergy syndrome (oral/perioral pruritus associated with food-specific immunoglobulin E)¹

- Dietary protein proctitis/proctocolitis of infancy²
- Dietary protein-induced enteropathy of infancy²
- Celiac disease²
- Dietary protein-induced enterocolitis of infancy²
- Occult blood loss from the gastrointestinal tract of milk-fed infants²

Subset with food allergy, evaluation often warranted

- Gastroesophageal reflux in infants³
- Eosinophilic esophagitis, any age group³
- Eosinophilic gastroenteritis³
- Enteropathy/malabsorption, any age group²

Possible relationship in subset, not well studied

- Constipation in early childhood
- Infantile colic

¹Associated with positive tests for food-specific immunoglobulin E antibody

²Characteristically not associated with positive tests for food-specific immunoglobulin E antibody

³Subtypes may be associated with positive tests for food-specific immunoglobulin E antibody

It is clear that in many disorders, a lack of response to treatments other than food elimination, and even a successful response to medical or surgical treatment, does not necessarily exclude food allergy as a cause for the condition.

The type of evaluation used for particular disorders is specific for each disorder and beyond the scope of these guidelines. However, an evaluation for food allergies may be undertaken initially, concomitantly with other diagnostic tests, or following failure to discern other causes, depending on the particular disorder and clinical history. In some cases, a particular finding during the evaluation may provide information that then prompts an evaluation for food allergy (i.e., >7 eosinophils per high-power field on esophageal biopsy).

Even without performing adjunctive laboratory tests, "formula changes" are commonly undertaken by pediatricians and families as a test of intolerance or allergy. There have been no specific guidelines concerning these formula changes. It is helpful to know that only a small proportion of infants with immunoglobulin (Ig) E-mediated cow's milk allergy (14%) will react to soy. In contrast, those with non-immunoglobulin E-mediated cow's milk allergy are frequently (>50%) reactive to soy protein. For these infants, a switch to extensively hydrolyzed cow's milk-based formula is the treatment of choice. For a small proportion of infants with symptoms that continue on hydrolysate, amino-acid based formula may be required. Breast-feeding is clearly cost-effective compared with infant formula, but maternally ingested protein can elicit allergic symptoms in the breast-fed infant. Maternal dietary manipulation (e.g., avoidance of milk protein) can be

undertaken for treatment in breast-fed infants, but with multiple food-allergic infants it may be difficult, and substitution with infant formulas may be needed.

The laboratory testing undertaken in the evaluation of food allergy includes both tests that are specific for food allergy and ancillary tests that are performed in the diagnostic evaluation of gastrointestinal symptoms, as listed in Table 4 of the original guideline document. This table also lists tests that are unproven and should not be used. Two factors that may guide the use of tests for food-specific immunoglobulin E antibody are the chronicity of symptoms and the association of atopic diseases (asthma, atopic dermatitis, and anaphylaxis to foods). In patients with acute reactions associated with particular food ingestions and those with chronic gastrointestinal symptoms who have other manifestations of atopic disease, tests for specific immunoglobulin E antibody (radioallergosorbent tests [RASTs] or skin-prick tests) are likely to be useful adjuncts for diagnosis, although the false-positive rate for predicting clinical symptoms of these tests is high. Similarly, for some of the disorders (eosinophilic gastroenteritis or eosinophilic esophagitis), a subset of patients may have positive tests for immunoglobulin E antibody. Lastly, tests for specific immunoglobulin E antibody may be needed to rule out the potential for severe acute reactions before conducting oral challenges in settings where patients have atopic diseases or possible history of acute reactions. In chronic disorders not associated with atopic disease, tests for food-specific immunoglobulin E are typically negative.

Ultimately, the diagnosis of food allergy rests on both the evidence of elements listed above and in Table 1 of the original guideline document and confirmation of reactivity/association determined by:

1. resolution of symptoms with an elimination diet, and
2. recurrence of symptoms after oral challenge (if challenge is appropriate in the particular setting).

Three approaches to dietary elimination include the following:

- Elimination of one or several specific foods associated with symptoms [useful for acute reactions, immunoglobulin E-positive foods, or high-suspicion food(s)].
- Oligoantigenic diet-specified foods allowed in the diet selected for generally low-risk for food allergy (useful when a large number of foods are associated with symptoms; however, can result in false-negative result if correct foods not eliminated).
- Elemental diet-hypoallergenic formula (i.e., amino acid-based formula) serves as total nutrition, may allow a few "safe" solids (useful when large number of foods is suspected or for infants on no or few solids; however, poor compliance outside of infancy).

The choice of dietary approach will depend on the specific history, whether a few or multiple foods are suspected, and likelihood of patient compliance. In identifying potential food allergens, it is useful to bear in mind that a rather short list of foods accounts for 85%-90% of significant reactions, although any food can provoke a reaction. Foods responsible for the majority of significant food allergy in infants, children, and adults are as follows:

Infants: Cow's milk; soy

Children: Cow's milk; egg; peanut; soy; wheat; tree nuts (walnut, hazel, etc); fish; shellfish

Adults: Peanut; tree nuts; fish; shellfish

Elimination of the causal protein should result in resolution of symptoms, although the time to resolution may be prolonged in some disorders (weeks in eosinophilic esophagitis). In some cases, adjunctive tests such as endoscopy/biopsy may be helpful to show resolution of pathology.

A general approach to the diagnosis of food allergy incorporating history, diagnostic tests, elimination diets, and challenge (see Table 7 of the original guideline document) is outlined in Figure 1 of the original guideline document, but a variety of adjustments in approach may be warranted for particular disorders/symptom complexes as described in the accompanying technical review and as mentioned above for infants. Specific information concerning procedures for performing oral food challenges is given in the accompanying technical review.

CLINICAL ALGORITHM(S)

An algorithm is provided for evaluating the role of food allergy in gastrointestinal disorders.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

To develop recommendations for evaluating the possibility of food allergy in patients with various clinical syndromes/symptoms, the guideline and accompanying technical review highlight results from larger, controlled studies; approaches from placebo-controlled, blinded studies; and consensus panel reports.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Food allergy is not one particular disorder, but rather immunopathophysiologic mechanisms underlying a number of defined or poorly defined gastrointestinal disorders/symptom complexes. Identification and elimination of the causal allergenic food protein from the diet can lead to resolution of symptoms.

Subgroups Most Likely to Benefit:

Infants and children

POTENTIAL HARMS

Oral food challenges can elicit severe anaphylactic reactions, so the physician must be comfortable with this potential for reaction and be prepared with emergency medications and equipment to treat such a reaction promptly.

Subgroups Most Likely to be Harmed:

- Severe anaphylaxis after the isolated ingestion of a food, with evidence of specific immunoglobulin E antibody to the causal food, is one clear example of a relative contraindication for oral challenge (although this is individualized because follow-up challenge for determination of resolution of allergy may be appropriate in some settings).
- Patients considered at "high risk" for anaphylactic reactions to oral challenge include those with positive tests for food-specific immunoglobulin E antibodies, those with previous severe reactions, asthmatic patients, and patients with enterocolitis syndrome.

QUALIFYING STATEMENTS

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The lack of standard approaches to evaluate food allergy, overlap of clinical manifestations of various disorders, the preponderance of case reports or small, uncontrolled studies, and deficiencies in study design frequently limited the conclusions that could be drawn and precluded meta-analyses.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: guidelines for the evaluation of food allergies. *Gastroenterology* 2001 Mar; 120(4):1023-5.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Nov 12 (reviewed 2001)

GUIDELINE DEVELOPER(S)

American Gastroenterological Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice and Practice Economics Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

According to the guideline developer, the Clinical Practice Committee meets 3 times a year to review all American Gastroenterological Association guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

This guideline has been reviewed by the developer and is still considered to be current as of Dec 2001.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Hugh A Sampson, MD; Scott H. Sicherer, MD; and Audrey H. Birnbaum, MD. AGA technical review on the evaluation of food allergy in gastrointestinal disorders. *Gastroenterology*. 2001 Mar; 120(4): 1026-40 [130 references].

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

The following is also available:

- The American Gastroenterological Association standards for office-based gastrointestinal endoscopy services. *Gastroenterology*. 2001 Aug; 121(2): 440-443 [8 references].

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer on July 12, 2002.

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